US Army Medical Research and Materiel

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DNA Vaccines Against Tick-borne Flaviviruses

This invention provides two plasmid-based, candidate tick-borne encephalitis (TBE) DNA vaccines that express the premembrane (prM) and envelope (E) genes of Central European encephalitis (CEE) or Russian spring summer encephalitis (RSSE) viruses under the control of a cytomegalovirus early promoter. The vaccines elicit cross-protective immunity to CEE and RSSE viruses, in mice.

TBE occurs over a wide area of Europe and the former Soviet Union. The most frequent cause is infection by either the CEE or RSSE virus. The CEE and RSSE viruses are antigenically and genetically closely related to one another and often are considered subtypes of the same virus. However, they are borne by two different tick vectors and the RSSE virus generally causes a more severe disease than CEE virus. Since 1976, a formalin-inactivated, chick embryo-derived vaccine has been used in parts of Europe and the number of TBE cases has notably declined. Although the vaccine is being used successfully, its disadvantages include the requirement for large-scale production and purification of a highly infectious pathogen, the risk of incomplete inactivation of the virus, and vaccination with adjuvant in a three-shot series. The vaccine is not licensed for use in U.S. military personnel nor in U.S. travelers to TBE-endemic regions.

The vaccine described in the invention was shown to be 100% effective in the mouse model for TBE. Sera from [illegible]s receiving the combined CEE and RSSE vaccines had Enzyme-Linked Immunosorbent Assay (ELISA) titers to CEE and RSSE antigens and neutralizing antibody titers to CEE virus equivalent to those elicited by the 1976 licensed vaccine. As neutralizing antibodies are a known [illegible] of protective immunity, it is likely the DNA [illegible]s could protect humans from TBE caused by CEE and RSSE.

Features and advantages:

- **Induces humoral immune response when delivered via a gene gun**
- **Vaccine is expressed in epidermis which is a focus of viral replication after tick bites**
- **Vaccine may be adapted for delivery to mucosal tissue**
- **Could provide an inherently safe human vaccine that would not result in adverse side effects**
- **Vaccine does not require growth or use of TBE, and thus avoids accidental**

Patent Status

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Point of Contact

Dr. Paul C. Mele
Director, Office of Research and Technology Applications
USAMRMC, MCMR-ZA-J
504 Scott St., Ft. Detrick, MD 21702-5012
E-mail: usamrmcorta@amedd.army.mil
Voice: 301-619-6664/2065/7219
Fax: 301-619-5034

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